UNIFORMED SERVICES UNIVERSITY
of the Health Sciences

Key Ethical Considerations in PTSD and TBI Research

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Center for the Study of Traumatic Stress

Disclaimer

- This presentation is based on personal observation. The opinions expressed should not be taken as representing the policy of the Uniformed Services University of the Health Sciences, the U.S. Army Medical Research and Materiel Command, or any other Government entity.

Why This Is a Critical Issue

- There are major gaps in our understanding of PTSD and TBI.
- DoD will be managing many new research projects, both internal and extramural.
- There is strong public and Congressional interest in PTSD and TBI.
- We owe our veterans the best possible research programs and protection for those who participate in our research programs.
- Managing this will be a challenge, and we should expect (and invite) scrutiny.

Scope of the Problem

- Over 1.6 Million service members have served in OEF/OIF. By December, 2007 837K of these had left active duty and are eligible for VA care.
- According to VA statistics, as of December 31 2007, diagnoses of OEF/OIF veterans included 133K+ with mental disorders and 124K+ with “symptoms, signs, and ill-defined conditions.”
- Most common mental disorders were PTSD (67.5K), Nondependent Abuse of Drugs (54.4K), and Depressive Disorders (45.1K), Neurotic Disorders (35.6K), Affective Psychoses (25.4K and Alcohol Dependence Syndrome (11.2K)

Scope of the Problem (Cont.)

- MHAT studies show that many veterans of OEF/OIF have mental health symptoms, of which PTSD is the most prominent.
- Repeated deployments are exacerbating the problem.
- Many are reluctant to seek care, or perceive barriers to obtaining care.
- The nation will be dealing with the mental health of veterans for many years. Most OEF/OIF veterans are under the age of 40.

Public Scrutiny

- The public and the media are very interested in the mental health of veterans.
- We should welcome this. It is an opportunity to care for our veterans.
- We may not always perceive media coverage as fair, but our task is to do the right thing. We can’t control what others say, but our best defense is having done our task well.

The Washington Times

WEATHER: BREEZY WITH SUNSHINE – HIGH 80, LOW 60 TUESDAY, JUNE 17, 2008 washingtontimes.com 50¢

Veterans

"You're a lab rat for $30 a month."
– James Elliott, a decorated Army sharpshooter

VA testing drugs on war veterans

Experiments raise ethical questions

By Audrey Hudson
THE WASHINGTON TIMES

The government is testing drugs with severe side effects like psychosis and suicidal behavior on hundreds of military veterans, using small cash payments to attract patients into medical experiments that often target distressed soldiers returning from Iraq and Afghanistan, a Washington Times/ABC News investigation has found.

Exclusive

In one such experiment involving the controversial anti-smoking drug Chantix, the Department of Veterans Affairs (VA) took three months to alert its patients about severe mental side effects. The warning did not arrive until after one of the veterans taking the drug had suffered a psychotic episode that ended in a near lethal confrontation with police.

Disposable HEROES

James Elliott, a decorated Army sharpshooter who suffers from post-traumatic stress disorder (PTSD) after serving 15 months in Iraq, was confused and psychotic when he was Tasered by police in February as he reached for a concealed handgun when officers responded to a 911 call at his Maryland home.

Mr. Elliott, a chain smoker, began taking Chantix last fall as part of a VA experiment that specifically targeted veterans with PTSD, opting to collect $30 a month for enrolling in the clinical trial because he needed cash as he returned to school. He soon began suffering hallucinations and suicidal thoughts, unaware that the new drug he was taking could have caused them.

Just two weeks after Mr. Elliott began taking Chantix in November, the VA learned from the Food and Drug Administration (FDA) that the drug was linked to a large number of hallucinations, suicide attempts and psychotic behavior. But the VA did not alert Mr. Elliott before his own episode in February.

In failing to do so, Mr. Elliott said, the VA treated him like a "disposable hero."

"You're a lab rat for $30 a month," Mr. Elliott said.

One of the nation's premier medical ethicists said the VA's behavior in the anti-smoking study violated basic protections for humans in medical experiments.

» see CHANTIX, page A14

ROD LAMKEY JR./THE WASHINGTON TIMES

STILL SMOKING: Iraq war veteran James Elliott smokes on his porch in Silver Spring as he talks about his experiences in war and dealing with post-traumatic stress disorder. Mr. Elliott suffered a psychotic episode while taking the anti-smoking drug Chantix.

BY THE NUMBERS

A Washington Times/ABC News 15-week investigation of military veterans being used as test subjects in government-sponsored clinical studies produced some startling numbers.

300: Number of studies on post-traumatic stress disorder (PTSD)

25: Number of drug tests on veterans with PTSD

5: Number of test drugs with warnings about suicide or suicidal thoughts

830,000: Number of veterans with PTSD

300,000: Number of veterans returning from Iraq or Afghanistan with depression or PTSD

40,000: Number of troops diagnosed with PTSD since 2003

4,796: Number of veterans enrolled in PTSD studies

2,488: Number of enrolled veterans returning from Iraq or Afghanistan

940: Number of veterans enrolled in a smoking cessation study

143: Number of veterans in a study taking Chantix, a drug linked to psychotic side effects

21: Number of veterans reporting adverse side effects while taking Chantix.

$11 million: Cost of the government anti-smoking study

Sources: Army surgeon general; Rand Corp., Veterans Affairs, Food and Drug Administration, National Institutes of Health, Institute for Safe Medication Practices

The Washington Times

A WHISPER OF A WARNING

In a Feb. 29 letter to participants in a smoking cessation study, the Department of Veterans Affairs watered down warnings about side effects from use of the drug Chantix, three months after the Food and Drug Administration issued its first alert about the drug. However, in a separate document, the VA revised its consent form for the study to provide a detailed warning about the drug's potentially fatal side effects.

DEPARTMENT OF VETERANS AFFAIRS

Date: February 29, 2008

RE: The Smoking Cessation and PTSD Study (CSP #519)

One of these medications is called varenicline, or Chantix.

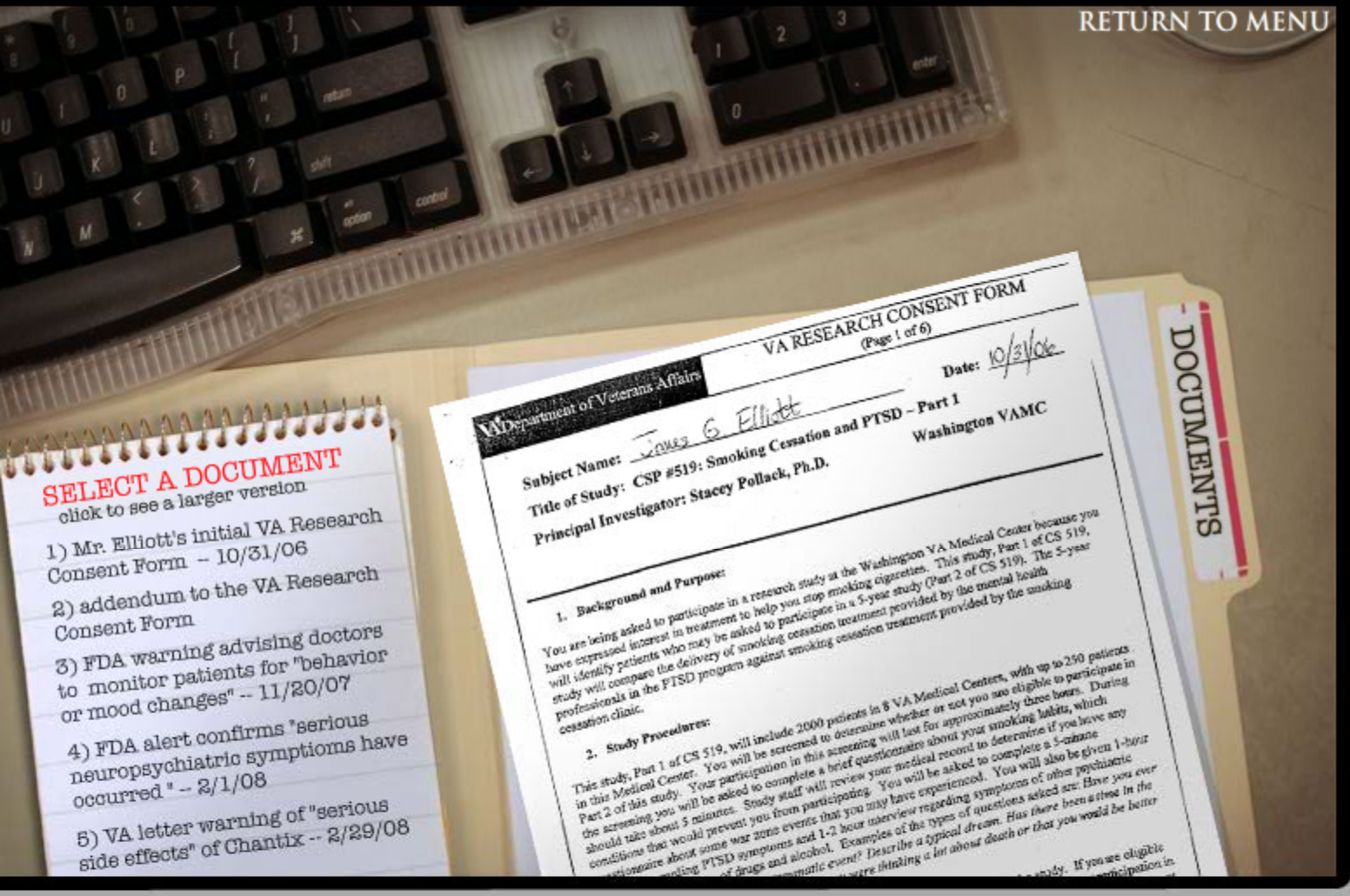
Scientists have recently learned that varenicline can sometimes have serious side effects in some people. These side effects may include an increase in psychiatric symptoms such as anxiety, nervousness, tension, and depression as well as untoward changes in behavior. It is important for you to know about the new risks of using

When you agreed to participate in the study you were told that you would be informed of any new information that became available. There is new information about varenicline that you should know. **Scientists have recently found that varenicline may also cause serious side effects in some people. These side effects include changes in behavior, anxiety, nervousness, tension, depression, thoughts of suicide, and attempted and completed suicide. Varenicline may make current psychiatric symptoms that you are experiencing worse, or may make old psychiatric symptoms return. In most cases, people had these side effects while taking varenicline, but some experienced them after stopping varenicline.**

The Washington Times

Disposable Heroes"

une 16



'Disposable Heroes': Veterans Used To Test Suicide-Linked Drugs

An ABC News and Washington Times Investigation Reveals Vets Are Being Recruited for Government Tests on Drugs with Violent Side Effects

By BRIAN ROSS and VIC WALTER
June 17, 2008

Mentally distressed veterans from Iraq and Afghanistan are being recruited for government tests on pharmaceutical drugs linked to suicide and other violent side effects, an investigation by ABC News and "The Washington Times" has found.

James Elliott and his fiancee tell Brian Ross about his experience on Chantix.

The report will air on "Good Morning America" and will also appear in "The Washington Times" on Tuesday. (click here to read "The Washington Times" coverage of "Disposable Heroes")

In one of the human experiments, involving the anti-smoking drug Chantix, Veterans Administration doctors waited more than three months before warning veterans about the possible serious side effects, including suicide and neuropsychiatric behavior.

"Lab rat, guinea pig, disposable hero," said former US Army sniper James Elliott in describing how he felt he was betrayed by the Veterans Administration.

Elliott, 38, of suburban Washington, D.C., was recruited, at $30 a month, for the Chantix anti-smoking study three years after being diagnosed with Post Traumatic Stress Disorder. He served a 15-month tour of duty in Iraq from 2003-2004.

VA Response to Media Reports

- In a press release on June 17, 2008, the VA pointed out that
  - The use of Chantix was within FDA guidelines and that the FDA has never asked that Chantix be removed from the market
  - The VA promptly informed health care providers of the FDA's early communication of possible side effects of Chantix.
  - The VA took great care in communicating the risks to patients and directed them to their providers.
  - The modest payment is in line with common practice.
  - Smoking is a serious health threat to veterans.

PTSD: Survey Research

- The main risks of survey research:
  - Participants may experience distress as a result of taking the survey.
  - Breaches of confidentiality could cause great harm
  - Group level risks, e.g., stigma for members of specific units or people who were in a particular operation.

Survey Participant Distress

- This risk, while legitimate, is often exaggerated
- Myths:
  - That surveys will bring on serious symptoms such as flashbacks
  - That being in research is inherently painful for trauma victims

Survey Participant Distress (Cont.)

- Facts
  - No evidence that people are damaged by trauma surveys.
  - In general symptoms such as flashbacks are linked to situations or media presentations (e.g., TV, movies) that share common features with the original trauma, not surveys.
  - However, a minority may upset by items on surveys.
  - Need more research, but existing research suggests that most participants appreciate being in research.

Survey Participant Distress (Cont.)

- It is essential to protect those participants who might be distressed
  - Informed consent must make the purpose and scope of the survey clear and warn that some items might be upsetting.
  - Care resources should be available on-site (if applicable) and a contact telephone number for a counselor should be provided.
  - Information for self-referral is appropriate, especially in military populations.

Confidentiality

- Breach of confidentiality can lead to great social, economic, legal, career, and/or family harm.
- Must ensure adequate measures to protect, e.g.,
  - Physical security, e.g., locked storage, limited access
  - Encrypted data
  - Coding of participant ID
  - Web survey must be on secure site. This is more than simply using an https:// site. See AR 25-2, Ch. 5.
  - Collect data in a way that does not pinpoint ID, e.g., ask questions with range options, e.g. age 20-30 yrs
  - Care in reporting results to avoid inadvertent ID of individuals/units even though no names were used

Confidentiality (Cont.)

- Consider whether you really need individual ID or can data be collected anonymously.
- Consider waiver of documentation of informed consent if that documentation is the main risk to confidentiality.
- No guarantee that data cannot be subpoenaed by courts or Congress. Participants must be informed of this risk of loss of confidentiality.
- Consider NIH Certificate of Confidentiality, especially if survey includes questions about drugs, family abuse or other legal issues.

Other Considerations for Surveys

- Consider risks to third parties, e.g., family or units, in survey research.
- Special care must be taken to avoid coercion if soldiers are recruited /enrolled in groups.
- If a mailed or electronic survey, consider providing for referral if participants feel they need assistance, e.g. “Military One Source” contact information or link.
- Inform participants that if they write in requests for help or indicate they may harm selves or others, confidentiality may need to be breached.

Treatment Research

- All groups must receive care. Standard of Care should be identified.
- Delay in treatment may be permissible to allow comparison or placebo groups.
- Should have manual for care to ensure fidelity to treatment plan.
- Need adequate inclusion/exclusion criteria, especially if recruiting participants who are already in treatment
- Need specific stopping rules

Treatment Research (Cont.)

- Treatment adequacy must be assessed.
- Safety plan should include rescue intervention.
- Medications - Off Label? Is IND needed?
- Confidentiality issues apply with treatment research too.

General Considerations for PTSD Research

- PTSD may be co-morbid with many disorders, e.g., depression.
- Expect AE's and SAE's, not necessarily study related, because the population is at high risk for reasons independent of the research.

TBI Intervention Research

- 10 USC 980 applies: If the subject is not competent to consent, then there must be intent to benefit for ALL study participants in all arms.
- Protocol must address potential for impaired decision capacity:
  - Need a specific plan to determine capacity to consent
  - If subject lacks capacity, must have a Legally Authorized Representative + Adult subject assent
  - Must adhere to state laws for LAR
  - Consent capacity may change; reassess at intervals

TBI Intervention Research (Cont.)

- Point of Injury studies may include enrolling people lacking capacity to consent and with no available LAR. These require Community Consultation (21 CFR 50.24) + Component Secretary waiver.
- Rehabilitation studies have all the issues of PTSD treatment studies discussed above.

Questions?
Comments?